

AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method for identifying a binding analog for a morphogen receptor ~~of a morphogen~~, said morphogen ~~being characterized as sharing at least 60% amino acid sequence identity or at least 70% amino acid sequence homology to with the sequence of~~ the C-terminal 102 amino acids of SEQ ID NO: 7, and being able to substitute for OP-1 in binding to a protein comprising SEQ ID NOs. 4, 6, or 8, said binding analog ~~being characterized as~~ having substantially the same binding affinity for said morphogen receptor as said morphogen, the method comprising:
  - (a) providing a sample without a Type II serine/threonine kinase morphogen receptor but containing a protein selected from:
    - (i) a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2), or an OP-1-binding receptor analog thereof;
    - (ii) a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3), or an OP-1-binding receptor analog thereof;
    - (iii) a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6), or an OP-1-binding receptor analog thereof;
    - ~~(iv) a polypeptide chain having binding affinity for OP-1 and sharing at least 40% amino acid identity with residues 23-122 of SEQ ID NO: 8 (ALK-6);~~
    - ~~(v) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid obtainable by amplification with one or more primer sequences defined by SEQ ID NOs: 12-15; or~~
    - ~~(vi)~~(iv) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid that hybridizes under a stringent conditions with a nucleic acid comprising the sequence defined by nucleotides 256-552 of SEQ ID NO: ~~8-7~~ (ALK-6), wherein the stringent condition has substantially the same stringency as when performing hybridization in 40% formamide, 5

X SSPE, 5X Denhardt's Solution, 0.1% SDS at 37°C overnight, then washing in 0.1 X SSPE, 0.1% SDS at 50°C;

- (b) contacting said sample with a candidate morphogen receptor-binding analog; and
- (c) detecting specific binding between said candidate morphogen receptor-binding analog and said protein;

wherein binding of said candidate morphogen receptor-binding analog to said protein is indicative that said candidate analog is a morphogen receptor-binding analog.

2. **(Currently Amended)** A method for identifying a binding analog of an OP-1 receptor ~~receptor-binding analog~~, said analog being characterized as having substantially the same binding affinity for a cell surface receptor as OP-1, the method comprising:

- (a) providing a cell that expresses a surface receptor protein having binding specificity for OP-1 selected from :
  - (i) a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2), or an OP-1-binding receptor analog thereof;
  - (ii) a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3), or an OP-1-binding receptor analog thereof;
  - (iii) a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6), or an OP-1 binding receptor analog thereof;
  - ~~(iv) a polypeptide chain having binding affinity for OP-1 and sharing at least 40% amino acid identity with residues 23-122 of SEQ ID NO: 8 (ALK-6);~~
  - ~~(v) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid obtainable by amplification with one or more primer sequences defined by SEQ ID NOs: 12-15; or~~
  - ~~(vi)~~(iv) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid that hybridizes under a stringent conditions with a nucleic acid comprising the sequence defined by nucleotides 256-552 of SEQ ID NO: 8 7 (ALK-6), wherein the stringent condition has substantially the

same stringency as when performing hybridization in 40% formamide, 5 X SSPE, 5X Denhardt's Solution, 0.1% SDS at 37°C overnight, then washing in 0.1 X SSPE, 0.1% SDS at 50°C;

- (b) contacting said cell with a candidate OP-1 receptor-binding analog; and
  - (c) detecting induction of an OP-1-mediated cellular response;
- wherein detection of induction of said OP-1-mediated cellular response is indicative that said candidate analog is an OP-1 receptor-binding analog.
- 3. **(Previously presented)** The method of claim 2 wherein said OP-1 mediated cellular response detected in step (c) is induction of a kinase activity, inhibition of epithelial cell growth, or induction of a cell differentiation marker.
  - 4. **(Previously presented)** The method of claim 2 or 3 wherein said cell comprises a transfected nucleic acid comprising a reporter gene in operative association with a control element derived from an OP-1 inducible protein, and wherein the activity of said reporter gene can be detected as said OP-1-mediated cellular response upon stimulation by OP-1 or analog thereof in said cell.
  - 5. **(Previously presented)** The method of claim 2 or 3, wherein said surface receptor protein further comprises part or all of a Type II serine/threonine kinase receptor protein having binding affinity for OP-1, activin or BMP-4.
  - 6-7. **(Canceled)**
  - 8. **(Currently Amended)** A kit for identifying OP-1 or a candidate OP-1 receptor binding analog in a sample, the kit comprising:
    - (a) a receptacle adapted to receive said sample, said receptacle containing a protein selected from:
      - (i) a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2), or an OP-1-binding receptor analog thereof;
      - (ii) a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3), or an OP-1-binding receptor analog thereof;

- (iii) a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6), or an OP-1 binding receptor analog thereof;
- ~~(iv) a polypeptide chain having binding affinity for OP-1 and sharing at least 40% amino acid identity with residues 23-122 of SEQ ID NO: 8 (ALK-6);~~
- ~~(v) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid obtainable by amplification with one or more primer sequences defined by SEQ ID NOs: 12-15; or~~
- ~~(vi)~~(iv) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid that hybridizes under a stringent conditions with a nucleic acid comprising the sequence defined by nucleotides 256-552 of SEQ ID NO: 8 7 (ALK-6), wherein the stringent condition has substantially the same stringency as when performing hybridization in 40% formamide, 5 X SSPE, 5X Denhardt's Solution, 0.1% SDS at 37°C overnight, then washing in 0.1 X SSPE, 0.1% SDS at 50°C; and
- (b) means for detecting induction of an OP-1-mediated cellular response as a means for detecting interaction of OP-1 or a candidate OP-1 receptor-binding analog with said protein of part (a), said OP-1 or candidate analog comprising part of said sample provided to said receptacle.

9. **(Canceled)**

10. **(Previously presented)** The kit of claim 8, further comprising a serine/threonine Type II receptor having binding specificity for OP-1, activin or BMP-4.

11-27. **(Canceled)**

28. **(Previously presented)** The method of claim 1, wherein said morphogen is OP-1.

29. **(Previously presented)** The method of claim 1, wherein said morphogen is 60A, DPP, OP-2, OP-3, BMP-2, BMP-4, BMP-5, BMP-6, Vgl, GDF-1, or Vgr-1.

30. **(Previously presented)** The method of claim 4, wherein said surface receptor protein further comprises part or all of a Type II serine/threonine kinase receptor protein having binding affinity for OP-1, activin or BMP-4.
31. **(Currently Amended)** A kit for identifying a binding analog for a morphogen receptor ~~of a morphogen~~ in a sample, said morphogen being characterized as sharing at least 60% amino acid sequence identity or at least 70% amino acid sequence homology ~~to~~ with the sequence of the C-terminal 102 amino acids of SEQ ID NO: 7, and being able to substitute for OP-1 in binding to a protein comprising SEQ ID NOs. 4, 6, or 8, the kit comprising:
- (a) a receptacle adapted to receive said sample, said receptacle does not contain a Type II serine/threonine kinase morphogen receptor but contains a protein selected from:
    - (i) a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2), or an OP-1-binding receptor analog thereof;
    - (ii) a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3), or an OP-1-binding receptor analog thereof;
    - (iii) a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6), or an OP-1 binding receptor analog thereof;
    - ~~(iv) — a polypeptide chain having binding affinity for OP-1 and sharing at least 40% amino acid identity with residues 23-122 of SEQ ID NO: 8 (ALK-6);~~
    - ~~(v) — a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid obtainable by amplification with one or more primer sequences defined by SEQ ID NOs: 12-15; or~~
    - ~~(vi)~~(iv) a polypeptide chain having binding affinity for OP-1 and encoded by a nucleic acid that hybridizes under a stringent conditions with a nucleic acid comprising the sequence defined by nucleotides 256-552 of SEQ ID NO: ~~87~~ (ALK-6), wherein the stringent condition has substantially the same stringency as when performing hybridization in 40% formamide, 5

X SSPE, 5X Denhardt's Solution, 0.1% SDS at 37°C overnight, then washing in 0.1 X SSPE, 0.1% SDS at 50°C; and

- (b) means for detecting specific binding interaction of OP-1 or said candidate analog with said protein of part (a), said OP-1 or candidate analog comprising part of said sample provided to said receptacle.
32. **(Previously presented)** The method of claim 1, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2).
33. **(Previously presented)** The method of claim 1, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3).
34. **(Previously presented)** The method of claim 1, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6).
35. **(Previously presented)** The method of claim 2, wherein said surface receptor protein is a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2).
36. **(Currently amended)** The method of claim ~~1~~ 2, wherein said surface receptor protein is a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3).
37. **(Currently amended)** The method of claim ~~1~~ 2, wherein said surface receptor protein is a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6).
38. **(Previously presented)** The kit of claim 8 or claim 31, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 16-123 of SEQ ID NO: 4 (ALK-2).

39. **(Previously presented)** The kit of claim 8 or claim 31, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 24-152 of SEQ ID NO: 6 (ALK-3).
40. **(Previously presented)** The kit of claim 8 or claim 31, wherein said protein is a polypeptide chain comprising an amino acid sequence defined by residues 23-122 of SEQ ID NO: 8 (ALK-6).